

# Letter to the Editor

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## Letter by Pyrogianni and La Vecchia Regarding Article, “Artificially Sweetened Beverages and Stroke, Coronary Heart Disease, and All-Cause Mortality in the Women’s Health Initiative”

To the Editor:

Mossavar-Rahmani et al<sup>1</sup> reported an association between artificially sweetened beverages (ASBs;  $\geq 2$  per day) and stroke, coronary heart disease, and all-cause mortality in a cohort of 81 714 postmenopausal US women from the Women’s Health Initiative Observational Study.

However, residual confounding is a key issue in that study. Women reporting consumption of  $\geq 2$  ASBs per day were more frequently obese, hypertensive, current or past smokers, with a history of diabetes mellitus and cardiovascular disease. Table 2 shows a drastic fall in the hazard ratios after allowance for covariates, which suggests that more precise and valid adjustment for confounding would likely result in a further decrease of the association. The hazard ratio for stroke declined from 1.59 to 1.23 after multivariate analysis, that of coronary heart disease from 1.94 to 1.29, and total mortality from 1.53 to 1.16. In addition, there was no trend in risk with dose. Only 5.1% of women reported an intake of  $\geq 2$  ASBs per day. This may well introduce selection bias. The association with stroke was stronger for black women (114 events in total), but the number of events in Black women consuming  $\geq 2$  ASBs per day is likely to be very small, and hence selection bias becomes a serious issue. Further, the use of a nonvalidated questionnaire for assessing ASBs consumption makes information bias difficult to quantify.

With regard to mechanisms, a systematic review by Toews et al,<sup>2</sup> commissioned by the WHO, found no evidence that low-calorie sweeteners (LCS) have adverse effects on major cardiovascular disease risk factors. They indeed found a small beneficial effect of LCS on body mass index and fasting blood glucose. When used to replace sugars, LCS help in total energy intake reduction and in modest weight loss.<sup>3</sup>

Randomized controlled trials showed that systolic and diastolic blood pressure, the major risk factor for stroke, were either lower or unaffected with LCS intake, compared with sugar or placebo.<sup>2</sup> In addition, other randomized controlled trials that have investigated higher intakes of ASBs of 1 L/d or more for 6 months found favorable effects on liver and vascular fat, and no material impact on glycemia, blood cholesterol, and triglyceride levels.<sup>4</sup>

Thus, the current evidence supports no plausible mechanism of how ASBs could increase the risk of stroke, coronary heart

disease, or other cardiovascular disease in humans. Data from both observational studies and randomized controlled trials indicate that LCS do not negatively affect risk factors linked to cardiovascular disease, including blood pressure, blood lipids levels, glycemia, or body weight.<sup>2-4</sup> Other potential mechanisms discussed by Mossavar-Rahmani et al, and which stem primarily from animal studies, have not been confirmed in humans.<sup>5</sup> Therefore, selection, reverse causation and, mainly, residual confounding may partly or largely explain the reported associations.

## Disclosures

V. Pyrogianni is consultant Nutrition Science Director to the International Sweeteners Association (ISA). Dr La Vecchia is a member of the ISA Scientific Advisory Panel.

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